REMARKS

The amendments to delete SEQ ID NO: unique identifiers for the sequences in Table 5, page 23, and Table 9, page 50, were made in order to conform to the definition of amino acids given in 37 C.F.R. §1.821(a)(2), where it states "Amino acids are those L-amino acids commonly found in naturally occurring proteins and are listed in WIPO Standard ST.25 (1998), Appendix 2, Table 3. Those amino acid sequences containing D-amino acids are not intended to be embraced by this definition." On page 23, lines 3-11 refer to substitutions of amino acids in the peptide 965.10, presented in Table 9, page 50, with the formula "aK(X)VAAWTLKAAa-NH_2". This sequence is identical, except for the amidation of the C-terminal residue, to the first sequence under the column heading "**Synthetic**" in Table 5. Page 23, line 6, specifically states that this peptide is "flanked on each end by D-amino acids". Similarly, by convention well-known by those skilled in the art, polypeptide sequences containing one-letter symbols for amino acids in lower case designate the substitution of D-amino acids for naturally occurring L-amino acids with the same one-letter symbol. Therefore, the sequences in Tables 5 and 9 containing lower case one-letter designations for D-amino acids do not fall under the definitions of amino acid sequences requiring inclusion in the Sequence Listing. By the same reasoning, the amino acid sequences on page 20, lines 3 and 4 and page 41, lines 22 and 23 are excluded from this definition and were not included in the Sequence Listing.

Claims 78-83 are pending in this application. Claims 80, 81 and 82 have been amended. The amendments to claims 80, 81 and 82 insert the assigned identifiers for SEQ ID NOS: designated in these claims.

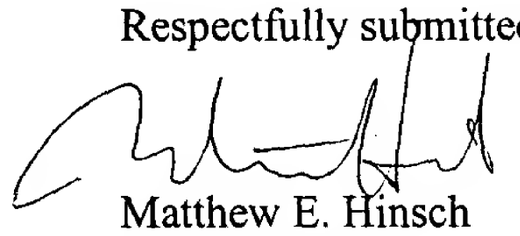
Applicants request entry of this amendment in adherence with 37 C.F.R. §§1.821 to 1.825. This amendment is accompanied by a floppy disk containing the above named sequences, SEQ ID NOS:1-25, in computer readable form, and a paper copy of the sequence information which has been printed from the floppy disk.

The information contained in the computer readable disk was prepared through the use of the software program "FastSEQ" and is identical to that of the paper copy. This amendment contains no new matter.

Attached hereto is a marked-up version of the changes made to the Specification and Claims by the current Amendment. The attached pages are captioned **"VERSION WITH MARKINGS TO SHOW CHANGES MADE."** As a convenience to the Examiner, a complete set of the Claims, as amended herein, is also attached to this Amendment as an Appendix entitled **"PENDING CLAIMS WITH ENTRY OF THE AMENDMENT."**

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Paragraph beginning at line 1 of page 23 has been amended as follows:

Examples of pan DR binding peptides of the invention that can induce or enhance a T-helper cell mediated immune response include, for example, the first 8 peptides listed in Table 9. This Table provides an illustration of various substitutions that one can make to obtain different pan DR stimulatory peptides. For example, the peptide 965.10 is a synthetic peptide, having a non-naturally occurring cyclohexylalanine or similar amino acid ~~peptide~~ at position X_2 and being flanked on each end by D-amino acids. An analogous preferred peptide has a substitution, *e.g.*, phenylalanine, at position X_2 of peptide 965.10. To obtain an all-natural yet analogous peptide, the D-amino acids at each end can be replaced by L-amino acids in addition to the substitution of a naturally occurring amino acid for the cyclohexylalanine; an all-L-amino acid peptide such as this can be prepared and/or administered using nucleic acids that encode the peptide. Each of these three peptides can then be subjected to an additional substitution at position X_6, as illustrated in Table 5. For example, the tryptophan at position X_6 of peptide 965.10 or its two derivatives can be replaced by asparagine, tyrosine, lysine, histidine, or alanine without loss of stimulatory activity. Thus, preferred peptides include those shown in Table 5.

Table 5

Amino acid at Position X_6	Synthetic	Replacement of Cyclohexylalanine	All-Natural (no D-amino acids or cyclohexylalanine)
W	aK(X)VAAWTLKAAa ~~(SEQ ID NO:11)~~	aKFVAAWTLKAAa ~~(SEQ ID NO:12)~~	AKFVAAWTLKAAA ~~(SEQ ID NO:13)~~ (SEQ ID NO:11)
N	aK(X)VAANTLKAAa ~~(SEQ ID NO:14)~~	aKFVAANTLKAAa ~~(SEQ ID NO:15)~~	AKFVAANTLKAAA ~~(SEQ ID NO:16)~~ (SEQ ID NO:12)
Y	aK(X)VAAYTLKAAa ~~(SEQ ID NO:17)~~	aKFVAAYTLKAAa ~~(SEQ ID NO:18)~~	AKFVAAYTLKAAA (SEQ ID NO:13) (SEQ ID NO:19)
K	aK(X)VAAKTLKAAa ~~(SEQ ID NO:20)~~	aKFVAAKTLKAAa ~~(SEQ ID NO:21)~~	AKFVAAKTLKAAA ~~(SEQ ID NO:22)~~ (SEQ ID NO:14)
H	aK(X)VAAHTLKAAa ~~(SEQ ID NO:23)~~	aKFVAAHTLKAAa ~~(SEQ ID NO:24)~~	AKFVAAHTLKAAA (SEQ ID NO:15) ~~(SEQ ID NO:25)~~
A	aK(X)VAAATLKAAa ~~(SEQ ID NO:26)~~	aKFVAAATLKAAa ~~(SEQ ID NO:27)~~	AKFVAAATLKAAA ~~(SEQ ID NO:28)~~ (SEQ ID NO:16)

Paragraph beginning at line 14 of page 41 has been amended as follows:

Peptides encompassing B-cell epitopes from the central immunodominant circumsporozoite repeat region of circumsporozoite proteins (CSP) of *P. yoelii* (PyB) or *P. falciparum* (PfB) were synthesized by standard MOC chemistry, purified by HPLC and their purity and identity verified by HPLC and mass spectrometry. Sequences: PyB = $G(QGPGAP)_4$ (SEQ ID NO:17) (Charoenvit, Y. *et al., J. Immunol.* **146**:1020-5 (1991)); PfB = $(NANP)_4$ (SEQ ID NO:18) (Nussenzweig, V. *et al., Adv Immunol* **45**:283-334 (1989); Dame, J.B. *et al., Science* **225**:593-9 (1984)). Peptides colinearly synthesized to encompass PADRE were also produced using the same methods. PADRE-PfB sequence: aKXVAAWTLKAa$(NANP)_4$GGS; PADRE-PyB sequence: aKXVAAWTLKAa$(QGPGAP)_4$GGS.

Paragraph beginning at line 25 of page 41 has been amended as follows:

A multiple antigen peptide (PyCSP-MAP) was also synthesized as previously described (Wang, R. *et al., J. Immunol* **154**:2784-93 (1995); Valmori, D. *et al., J Immunol Meth* **149**:717-21 (1992)). In brief, it included a lysine core and four branches. Each branch included four copies of the protective B-cell epitope, QGPGAP

(SEQ ID NO:19), from the PyCSP and the universal T-helper epitopes from tetanus toxin, p2p30 (p2 = QYIKANSKFIGITE (SEQ ID NO:5); p30 = FNNFTVSFWLRVPKVSASHLE (SEQ ID NO:20)) (Wang, R. *et al., J. Immunol* **154**:2784-93 (1995)).

Paragraph beginning at line 7 of page 46 has been amended as follows:

Encouraged by the data from the experiments shown above, we determined next if immunization with the PADRE-PyB peptide would protect mice against sporozoite challenge. In order to select a control immunogen we relied on the following information. We have previously reported that immunization with a multiple antigen peptide branched chain polymer including the 35 amino acid P2P30 universal T-cell epitope sequences from tetanus toxin, and four copies of the six amino acid tandem repeat (QGPGAP; SEQ ID NO:19) from the *P. yoelii* circumsporozoite protein (PyCSP) in multiple adjuvants induces high levels of antibodies that inhibit sporozoite invasion of hepatocytes *in vitro* and protect against sporozoite challenge *in vivo* (Wang, R. *et al., J. Immunol* **154**:2784-93 (1995)). We have also determined that doses of 25 μg of this PyCSP MAP induce higher levels of protection than do higher doses. Accordingly, this immunogen was used as a positive control in our experiments.

Paragraph (Table 8) beginning at line 3 of page 48 has been amended as follows:

Table 8

Antibodies and protective immunity after immunization of mice with PyCSP synthetic peptide vaccines

Immunogen/ Adjuvant	Infected/ challenged	% Protected	IFAT Sporozoites (titer[a] x 10-3)	ELISA $(QGPGAP)_2$[c] PyCS.1 (OD Units x 10-3)[b]	
PyB/Titermax™	7/8	12.5	-	-	-
PADRE-PyB/ Titermax™	2/8	75.0	3.2	25.6	25.6
PyCSP-MAP/ Titermax™	2/7	71.4	3.2	12.8	12.8
-/ Titermax™	7/8	12.5	-	-	-
Infectivity control	8/8	0	ND	ND	ND

[a]Titer is defined as the reciprocal of the last serum dilution yielding positive reactivity as detected by fluorescence microscopy. [b]The reciprocal of the serum dilution at which the optical density (410 nm) was 1.0. [c] $(QGPGAP)_2$ = SEQ ID NO:21

Paragraph (Table 9) beginning at line 1 of page 50 has been amended as follows(see attached sheet).

Table 9

Binding Activity of PADRE Analogs

PEPTIDE	SEQ ID NO.	SEQUENCE	DR1	DR2wB2	DR3	DR4w4	DR4w14	DR5	DR7	DRw53	DQ3.1
965.08	~~29~~	aK(X)VAANTLKAAa-NH_2	1.2 (1)	3.8	250	3	13.8	8	192.3	163.8	--
965.09	~~30~~	aK(X)VAAYTLKAAa-NH_2	0.8	7.4	250	1	7	5.4	192.3	86.4	--
965.10	~~31~~	aK(X)VAAWTLKAAa-NH_2	1.2	5.6	119	2.8	9.8	11.1	147.1	141.8	25
965.14	~~32~~	aK(X)VAAKTLKAAa-NH_2	3.6	8	781	7.4	62.5	3.4	227	52.8	--
965.15	~~33~~	aK(X)VAAHTLKAAa-NH_2	1.9	5.4	1389	3.2	13.8	29.9	156.3	79.2	--
965.16	~~34~~	aK(X)VAAATLKAAa-NH_2	4.2	6.1	1471	6.2	55.6	16.7	227	131.9	--
965.17	22 ~~35~~	AK(X)VAAWTLKAAA-NH_2	2	5.9	1786	3.8	26.7	9.1	147.1	169.6	--
553.01	5 ~~36~~	QYIKANSKFIGITE	51.5	20	2717	8036	10000	20	25	--	--
553.02	~~37~~	qYIKANSKFIGITEa	238	25.3	-- (2)	--	--	83.3	49	--	--

(1) = nM IC_{50} values
(2) dashes indicate >10,000 nM
(X) = cyclohexylalanine
"-NH_2" indicates amidation at the carboxyl terminus of the peptides.